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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/896,896	06/29/2001	Jens Sigurd Okkels	0217us210	1537

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MAXYGEN, INC.
INTELLECTUAL PROPERTY DEPARTMENT
515 GALVESTON DRIVE
RED WOOD CITY, CA 94063

EXAMINER	
LIU, SAMUEL W	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 02/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/896,896	OKKELS ET AL.	
	Examiner	Art Unit	
	Samuel W Liu	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-72* is/are rejected.

7)☒ Claim(s) *59 and 67* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10-9-01* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the claims

Claims 58-72 are pending.

The applicants' amendment filed 22 December 2003, which cancels claims 1-57 and add claims 58-72, and applicants' request (filed 22 December 2003) for extension of time of two months have been entered.

Election/Restrictions

In the response filed 22 December 2003, Applicant's election without traverse of Group IV, claims 45-57, is acknowledged. Yet, applicants have canceled claims 45-57. Therefore, the pending claims 58-72 are under examination in this Office action.

IDS

The references listed in IDS filed 9 October 2001 and IDS filed 25 June 2002 have been received and considered.

Specification/Claim/ Objections

The disclosure is objected to because of the following informalities:

(1) In page 19, line 17, "PEG" should be spelled out in full at the first instance of use.

(2) In claims 59 and 67, before "recovering ...", "c)" and "d)", should be deleted, respectively.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, the second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 58-72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 58, item a, recites "... a peptide ...which contributes to an in vivo glycosylation site" wherein "contribute to" is not clear as to whether or not the peptide participates in glycosylation by possessing the glycosylation site (*cis* action) or by an indirect mechanism wherein the peptide does not possess the glycosylation site but has an ability of stimulating or inhibiting glycosylation thereof (*trans* action). See also claim 60. Claim 58, item a, recites "X is a peptide addition 1-30 amino acids"; the recitation is unclear as to whether or not 1-30 amino acids are added to said peptide. See also claim 66. Claim 58 is unclear in the recitation "a peptide-extended polypeptide" (item a) and "a peptide-extended glycosylated polypeptide" (item b) because the specification does not define the recitations; does the item a) recitation refers to a polypeptide comprising branched peptide moiety (or moieties) attached to the peptide backbone of said polypeptide through isopeptide bond formed between lysine ε-amine group and carboxyl group? does the item b) recitation refers to a glycosylated polypeptide comprising branched peptide moiety (or moieties) attached to the peptide backbone of said polypeptide through isopeptide bond formed between lysine ε-amine group and carboxyl group? See also claims 59, 65-67 and 69-71. Further, recitation "Pp is the polypeptide of interest" (see the claim item a) is unclear; does it refer to any portion of said polypeptide of interest? The dependent claims are also rejected.

Claim 65 is unclear in "a non-peptide moiety" regarding whether or not said moiety refers to nucleotide, or polynucleotide, or organic polymer, or lipid, or lipid –polysaccharide

conjugate. The specification provides insufficient definition of the non-peptide moiety. See also claim 71. In addition, claim 65 is unclear in "an attachment group"; does said group differs form the glycosylation site? Or, does said group comprise several non-contiguous structural motifs that participate in glycosylation?

Claim 66 is indefinite in "one or more peptide-extended polypeptide". The claim sets forth a process of identifying a peptide-extended glycosylated polypeptide comprising *screening* said polypeptide. In view of the fact that the *screening* step requires at least two or more objects being subject to the screening, the claim language "one or more peptide-extended polypeptide" wherein the limitation "one" renders the claim indefinite. Claim 66 recites "elongation mutagenesis"; the recitation is unclear because without defining what the elongation mutagenesis means (note that the specification is silent in defining said recitation), one of ordinary skill in the art would not reasonably understand the claimed subject matter. Further, claim 66 is not apparent in recitation "such that" regarding to what extent the mutagenesis of the nucleic acids would produce the recombinant nucleic acids. The dependent claims are also rejected.

Claim 71 sets forth the limitation "the method of claim 69 further comprising reacting the peptide-extended glycosylated polypeptide with …". However, it appears that the limitation has no operative link to the method (claim 69 from which claim 17 depends) of making a peptide-extended glycosylated polypeptide. Thus, claim 71 is indefinite in this regard.

Claim 72 recites "serum half-life"; the recitation is unclear as to whether or not the "half-life" refers to metabolic half-life (*in vivo*) or chemical half-life (*in vitro*). Also, claim 72 recites "increased functional in vivo half-life"; the recitation is awkward because there is not object associated with "increased functional", *i.e.*, what is subject to functional increase. Additionally,

claim 72 recites "improve formulation"; the recitation is not apparent as to whether or the said formulation refers to formulation of pharmaceutical composition, or formulation for an immunoassay kit.

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 58-67 and 69-72 are rejected under 35 U.S.C. 102(b) as being anticipated by Sasaki, K. et al. (US Pat. No. 5218092).

Sasaki et al. teach a method of altering the glycosylation pattern of a glycoprotein, human granulocyte colony stimulating factor (hG-CSF) comprising (i) constructing a DNA encoding modified-glycoprotein (a protein of interest), and (ii) expressing the modified glycoprotein thereof (see "Summary of the Invention", column 5, lines 5-33, Figure 8, and column 24, lines 58-64). The said DNA comprises a polynucleotide segment encoding N-terminal glycosylation sequence "APTYRNSS" (see Table 3). This sequence meets the limitation "X" (a peptide comprising a glycosylation site) set forth in the formula: NH_2-X-Pp-*COOH* of claim 58. Also, this sequence meets the limitation "Pp" (the polypeptide of interest) because of its covalently linkage to a polypeptide of interest (see Table 3 sequence from residues 9 (Leu) to 174 (Pro)). Note that since the instant claims do not make it clear as to whether or not said polypeptide of interest is a full-length polypeptide or any *portion* of the polypeptide of interest, the polypeptide

portion of residues 9-174 of Table 3 sequence is regarded as "Pp", i.e., the polypeptide of interest. Therefore, Sasaki et al. patent meets the limitation set forth in the formula NH_2-X-Pp-*COOH*, and therefore anticipates the application claim 58.

Sasaki et al. teach expressing the above-mentioned cDNA in mammalian cells (see column 24, lines 62-64, and column 25, lines 36-43), as applied to the application claim 64.

Sasaki et al. teach that the said method (see the above statement) further comprises selecting the modified-glycoprotein that comprises N-terminal peptide having recombinantly-introduced glycosylation site(s) (see column 25, lines 49-62, and column 9, lines 1-3, and "summary of the Invention" at column 5), as applied to the application claim 66.

Sasaki et al. teach a method of making the modified-glycoprotein comprising preparing, expressing and selecting the recombinant polynucleotide that encodes the modified glycoprotein as stated above, and comprising producing the selected modified-glycoprotein (see Examples 4-5 and Figure 8), as applied to claim 69 of the instant application.

Sasaki et al. teach obtaining (i.e., recovering) the modified-glycoprotein from host cells that produce the glycoprotein thereof (see column 26, lines 13-21, and columns 13-15), as applied to claim 59 of the current application.

Sasaki et al. teach that the above-mentioned "APTYRNSS" (i.e., hG-CSF [ND28N6], see Table 3) comprises in vivo N-glycosylation site (see column 36, lines 50-68, and Example 5), as applied to the application claim 60.

The peptide "APTYRNSS" (i.e., hG-CSF [ND28N6], see Table 3) has the structural feature: X_1-N- X_2-[T/S]C-Z" as set forth in claim 61 and meets the limitation of claim 63. Thus,

Sasaki et al. anticipates the application claims 61 and 63. Since the formula for "X" motif set forth in claim 62 encompasses the formula of claim 61 (*i.e.*, the formula of claim 62 has broader scope than that of claim 61), the Sasaki et al. teaching anticipates the application claim 62 as well.

Sasaki et al. further teach the covalent attachment of a non-peptide moiety (carbohydrate-lipid conjugate) to the glycosylation site of the modified-glycoprotein (see column 2, lines 1-19), as applied to the application claims 65 and 71.

Also, Sasaki et al. teach a process of obtaining the modified-glycoprotein having improved properties, e.g., longer half-life in blood than those of a naturally occurring form (see abstract), as applied to the application claims 67 and 70.

Further, Sasaki et al. teaches that the modified-glycoprotein recombinantly-produced has increased plasma (blood) half-life because of enhanced resistance to proteolysis (see column 5, lines 18-23, and abstract). The Sasaki et al. teaching thus anticipates claim 72 of the instant application.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is 571 272-0949. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low, can be reached on 571 272-0951. The fax phone number for the organization where this

application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

SWL

Samuel Wei Liu, Ph.D.

February 3, 2004

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER